



1614  
PATENT  
Attorney Docket No. UM-08477

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Shaomeng Wang *et al.*

Serial No.: 10/729,156

Group No.: 1614

Filed: 12/05/2003

Examiner:

Entitled: Small Molecule Antagonists of BCL-2 Family Proteins

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STATEMENT TRANSMITTAL

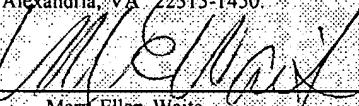
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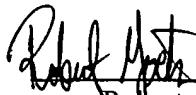
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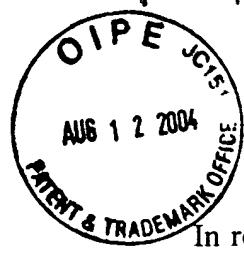
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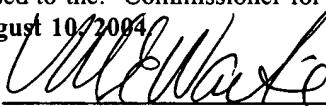
Entitled: **Small Molecule Antagonists of BCL-2 Family Proteins**

**INFORMATION DISCLOSURE STATEMENT**

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The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

- U.S. Patent No.
- U.S. Patent No. 3,364,242 issued on 1/16/68
- U.S. Patent No. 3,347,885 issued on 10/17/67
- U.S. Patent No. 4,297,341 issued on 10/27/81
- U.S. Patent No. 4,747,979 issued on 5/31/88
- U.S. Patent No. 4,806,568 issued on 2/21/89
- U.S. Patent No. 5,026,726 issued on 6/25/91
- U.S. Patent No. 5,059,717 issued on 10/22/91
- U.S. Patent No. 5,077,441 issued on 12/31/91

- U.S. Patent No. 5,112,637 issued on 5/12/92
- U.S. Patent No. 5,260,327 issued on 11/9/93
- U.S. Patent No. 5,277,909 issued on 1/11/94
- U.S. Patent No. 5,385,936 issued on 1/31/95
- U.S. Patent No. 5,759,837 issued on 6/2/98
- U.S. Patent No. 5,780,675 issued on 7/14/98
- U.S. Patent No. 6,113,397 issued on 9/5/2000
- U.S. Patent No. 6,576,660 issued on 6/10/03
- U.S. Patent No. 6,608,107 issued on 8/19/03
- U.S. Patent No. 2002/0137801A1 published on 9/26/02
- U.S. Patent No. 2003/0082101A1 published on 5/1/03
- U.S. Patent No. 2003/0119894A1 published on 6/26/03
  
- WO 02/41828 A2 30 May 2002
- WO 02/47673 A2 20 June 2002
- EP 0 651 636 B1 26 July 1993
- 1 917 341 3 April 1969
- 01132542 A 19 Nov. 1987
- CH 676360 A5 28/12/88
- SU 1351915 A1 16/6/82
  
- V. Amberger, *et al.*, Cancer Res., 58:149-158 (1998)
- Wick *et al.* (W. Wick, *et al.*, FEBS Lett., 440:419-424 (1998)
- S. Mohanam, *et al.*, Cancer Res. 53:4143-4147 (1993)
- P. Pedersen, *et al.*, Cancer Res., 53:5158-5165 (1993)
- Nuria Rubio, Lab Invest, 81:725-734 (2001)
- Fernández *et al.*, Cell Death Differ., 7:350-359 (2000)
- J. Reed, Nature, 387:773-776 (1997)
- S. Frisch and E. Ruoslahti, Curr. Opin. Cell Biol., 9:701-706 ((1997)
- D. Del Bufalo, *et al.*, FASEB J., 11:947-953 (1997)
- Razakantoanina *et al.* Parasitol. Res., 86:665-668 (2000)

- Dao *et al.* *Bioorg. Med. Chem.*, 11:2001-2006 (2003)
- Deck *et al.* *J. Med. Chem.*, 34:3301-3305 (1991)
- Przybylski *et al.* *J. Mol. Structure*, 611(1-3):193-201 (2002)
- R.E. Royer *et al.*, *J. Med. Chem.*, 38:2427-2432 (1995)
- R.E. Royer *et al.*, "Biologically active derivativse of gossypol: synthesis and antimalarial activities of peri-acylated gossylic nitriles:", *J. Med. Chem.*, 29:1799-1801 (1986)
- C.M. Venuti, *J. Org. Chem.*, 46(15):3124-3127 (1981)
- P.C. Meltzer *et al.*, *J. Org. Chem.*, 50(17):3121-3124 (1985)
- R. Adams *et al.*, *J. Am. Chem. Soc.*, 60:2193-2204 (1938)
- Le Blanc *et al.*, "An in vitro study of inhibitory activity of gossypol, a cottonseed extract, in human carcinoma cell lines", *Pharmacol. Res.*, 46:551-555 (2002)
- Baumgrass *et al.*, "Reversible inhibition of calcineurin by the polyphenolic aldehyde gossypol", *J. Biol. Chem.*, 276:47914-47921 (2001)
- Shelley *et al.*, "Structure-activity studies on gossypol in tumor cell lines," *Anticancer Drugs*, 11:209-216 (2000)
- Sonenberg *et al.*, "Anti-fertility and othe ractions of gossypol analogues", *Contraception*, 37:247-255, (1988)
- Whaley *et al.* ."Monkey lactate dehydrogenase-C4 as a model for the interaction of enzymes with gossypol", *Contraception*, 33:605-616 (1986)
- Dorsett *et al.*, "Letter: Antivtrial activity of gossypol and apogossypol", *J. Pharm. Sci.*, 64:1073-1075 (1975)
- Wu *et al.*, "Synthesis and antifertility actions of gossypol derivatives and phenol aldehydes", *Yao Xue Xue Bao*, 24:502-511 (1989)
- Hoffer *et al.*, "Antifertility, spermicidal and ultrastructural effects of gossypol and derivatives administered orally and by intratesticular injections", *Contraception*, 37:301-331 (1988)
- Guo *et al.*, "Synthesis of mono-aldehyde gossypol and its analogues", *Yao Xue Xue Bao*, 22:597-602 (1987)

- Manmade *et al.*, "Gossypol. Synthesis and in vitro spermicidal activity of isomeric hemigossypol derivatives", *Experientia*, 39:1276-1277 (1983)
- Dowd, *Chirality*, 15:486 (2003)
- Ciesielska *et al.*, *Chem. Phys. Lett.* 353:69 (2002)
- Vermel *et al.*, *Antitumour Activity of Gossypol in Experiments on Transplanted Tumours* 39-43 (1963)
- J.C. Reed, *Pharmacology*, 41:501-553 (1997)
- J.C. Reed *et al.*, *J. Cell Biochem.*, 6:23-32 (1996)
- Z. Han *et al.*, *Cancer Res.*, 56:621-628 (1996)
- S.W. Muchmore *et al.*, *Nature*, 381:335-341 (1996)
- A.M. Petros *et al.*, *Protein Sci.*, 9:2528-2534 (2000)
- A.M. Petros *et al.*, *Proc. Natl. Acad. Sci. U.S.A.*, 98:3012-3017 (2001)
- X.M. Yin *et al.*, *Nature*, 369:321-323 (1994)
- S.C. Cosulich *et al.*, *Curr. Biol.*, 7:913-920 (1997)
- A. Sali *et al.*, *Structure, Function, and Genetics*, 23:318-326 (1995)
- A. Sali, *Curr. Opin. Biotech.*, 6:437-451 (1995)
- J.L. Wang *et al.*, *Cancer Res.*, 60:1498-1502 (2000)
- J.L. Wang *et al.*, *Proc. Natl. Acad. Sci. U.S.A.*, 97:7124-7129 (2000)
- Sattler *et al.*, *Science*, 275:983-986 (1997)
- B.R. Brooks *et al.*, *J. Comp. Chem.*, 4,187-217 (1983)
- P.V.R. Schleyer *et al.*, *CHARMM: The Energy Function and Its Parameterization with an Overview of the Program*, in *The Encyclopedia of Computational Chemistry*, 1:271-277 eds., John Wiley & Sons, Chichester (1998)
- S. Makino and I.D. Kuntz, *J. Comput. Chem.* 18:1812-1825 (1997)
- I.J. Enyedy *et al.*, *J. Med. Chem.*, 44:313-4324 (2001)
- Leschev, "Influence of the Extract of *Eleutherococcus senticosus* on development of experimental pituitary adenomas in rats", *Institute of Oncology of the U.S.S.R. Academy of Medical Sciences*, 60-67 (1966)
- Willemsen, *An Oxazoline-Based Approach to the Total Asymmetric Synthesis of (S)-Gossypol*, UMI PROQuest Digital Dissertations - Full Citation & Abstract

- La Blanc *et al.*, An in vitro study of inhibitory activity of gossypol, a cottonseed extract, in human carcinoma cell lines, *Pharmacol. Res.* 46(6):551-5 (2002)
- Griffith *et al.*, Bioenvision Successfully Completes Formulation Research to Develop Gossypol as a Novel Anti-Cancer Agent, *Bioenvision News* (2003)
- Saydachmov *et al.*, Uebekskii Khimicheski Zhumal (1):11-13 (1994)
- Zakhidov *et al.*, Modifying Cytogenetic Effects of Gossypol and Derivatives, Library National Institutes of Health (1994)
- Yerukhimov, Treatment of Bladder Tumors With Gossipol And Ionol In Combination With Surgical Intervention, *Issues in Oncology*, XI (1966)
- Kuznezova *et al.*, *Pharmacol. Toxicol.*, Boston Library Boston Spa (1979)
- Zhong *et al.*, National Library of Medicine, 2:159-161 (1982)
- Zhang *et al.*, Inhibitory effects (-)-gossypol on proliferation and keratinocyte growth factor expression in human breast epithelial cells, stromal cells, and adipocytes, *American Association fro Cancer Research* 38:218 (1997)
- Zheng *et al.*, Gossypol (GP) Stimulates Transforming Growth Factor Beta (TGF- $\beta$ ) Gene Expression in Human Breast Cancer Cell Line, *The FASEB Journal* 10:A757 (1996)
- Zheng *et al.*, Studies on the Resolution of Racemic Gossypol, *ACTA Pharmaceutica Simica* 25(6):430-434 (1990)
- Adlakha *et al.*, Inhibition of DNA Polymerase  $\alpha$  And Ribonucleotide Reductase by By Gossypol, *Proceedings of AACR* 26:249:982 (1985)
- Akhila *et al.*, Biosynthesis of Gossypol in *Thespesia Populnea*, *Phytochemistry* 33:335-340 (1993)
- Badria *et al.*, Antimitotic Activity of Gossypol and Gossypolone, *Pharmaceutical Biology*, 39:120-126 (2001)
- P. Baille *et al.*, *Clin. Cancer Res.*, 3:1535-1538 (1997)
- Balci *et al.*, Gossypol induced apoptosis in the human promyelocytic cell line HL60, *Cytogenet Cell Genet* 85:5-181 (1999)
- Balci *et al.*, Gossypol Induced Apoptosis in the Human Promyelocytic Leukemia Cell Line HL 60, *Tohoku J. Exp. Med.* 189:51-57 (1999)

- Band *et al.*, Antiproliferative Effect Of Gossypol and Its Optical Isomers on Human Reproductive Cancer Cell Lines, *Gynecologic Oncology* 32:273-277 (1989)
- Band *et al.*, Cytocidal Effects of Gossypol and Its Optical Isomers on Reproductive Cancer Cell Lines, *Gynecologic Oncology* 23:261 (1986)
- Benz *et al.*, Lactic Dehydrogenase Isozymes,  $^{31}\text{P}$  Magnetic Resonance Spectroscopy, and In Vitro Antimitochondrial Tumor Toxicity with Gossypol and Rhodamine-123, *J. Clin.Invest.* 79:517-523 (1987)
- Benz *et al.*, Selective Toxicity of Gossypol Against Epithelial Tumors and its Detection by Magnetic Resonance Spectroscopy, *Contraception* 37:221-229 (1988)
- Benz *et al.*, Gossypol Enantiomers (+, -) Differentially Uncouple Tumor Mitochondria, Block Glutathione-S-Transferase Acitivity, and Inhibit Cellular Proliferation, *Proceedings of AACR* 29:322 (1988)
- Benz *et al.*, Biochemical Correlates of the Antitumor and Antimitochondrial Properties of Gossypol Enantiomers, *Molecular Pharmacology* 37:840-847 (11990)
- Benz *et al.*, Gossypol Effects on Endothelial Cells and Tumor Flow, *Life Sciences* 49:67-72 (1991)
- Blackstaffe *et al.*, Cytotoxicity of gossypol enantiomers and its quinone metabolite gossypolone in melanoma cell lines, *Melanoma Research* 7:364-372 (1997)
- Bourinbaiar *et al.*, Comparative in vitro study of contraceptive agents with anti-HIV activity: *Gramicidin, nonoxynol-9, and gossypol*, *Contraception* 49:131-137 (1994)
- Brandes *et al.*, New Drugs in Recurrent High Grade Gliomas, *Anticancer Research* 20:1913-1920 (2000)
- Brandes *et al.*, New therapeutic agents in the treatment of recurrent high-grade gliomas, *FORUM Trends in Experimental and Clinical Medicine* 10:121-131 (2000)
- R. Bruno *et al.*, *J. Clin. Oncol.*, 16:187-196 (1998)

- Bushunow *et al.*, Gossypol Treatment of Recurrent Adult Malignant-Gliomas, Proceedings of ASCO, 14:282 (1995)
- Bushunow *et al.*, Gossypol Treatment of recurrent adult malignant gliomas, Journal of Neuro-Oncology 43:79-86 (1999)
- Chang *et al.*, Antiproliferative and Antimetastatic Effects of Gossypol (GP) on Mat-Lylu-Bearing Rats, FASEB Journal, 6:3794 (1992)
- Chang *et al.*, Prostate, begin hypertrophy and prostatic carcinoma: A study of cell biology of prostate and chemotherapy for prostatic hypertrophy and prostatic cancer, Dissertation Abstract International, 55:4330-B (1995)
- Chang *et al.*, Potential of Gossypol (GP) and Transforming Growth Factor- $\beta$ , (TGF- $\beta$ <sub>1</sub>) as Inhibitors of Canine Prostate Growth, FASEB Journal, 9:4813-4814 (1995)
- Chang *et al.*, Antiproliferative and Antimetastatic Effects of Gossypol on Dunning Prostate Cell-Bearing Copenhagen Rats, Research Communications in Chemical Pathology and Pharmacology 79:293-312 (1993)
- Chen *et al.*, Application of 2D NMR Techniques in the Structure Determination of Ganosporelactone A and B, ACTA Pharmaceutica Sinica 26:430-436 (1991)
- Coyle *et al.*, *In-Vitrop* and *in vivo* cytotoxicity of gossypol against central nervous system tumor cell lines, Journal of Neur-Oncology 19:25-35 (1994)
- Dallacker *er al.*, Uber Gossypol- und Hemigossypol-Derivate - Darstellung von Hydroxy-methyl-naphto[1,3]dioxolen, Chemiker-Zeitung 113:5-11 (1989)
- Dallacker *et al.*, Darstellung von Methyl-isopropyl-naphthol-derivaten durch Pd-katalysierte Cyclocarbonylierung, Chemiker-Zeitung 114:144-147 (1990)
- Dao *et al.*, Synthesis and cytotoxicity of gossypol related compounds, Eur. J. Med. Chem. 35:805-813 (2000)
- Darzynkiewicz *et al.*, Cytometry in Cell Necrobiology: Analysis of Apoptosis and Accidental Cell Death (Necrosis), Cytometry 27:1-20 (1997)
- Data *et al.*, A Study of the Derivatives of ( $\pm$ )-Gossypol, Indian Journal of Chemistry 10:691-693 (1972)
- Davila *et al.*, Toxicological Studies of Gossypol in Primary Culture of Postnatal Rat Hepatocytes, Journal of Molecular and Cellular Toxicology, 4:161-170 (1991)

- Deck *et al.*, Gossypol and Derivatives: A New Class of Aldose Reductase Inhibitors, *J. Med. Chem.* 34:3301-3305 (1991)
- DeMartino *et al.*, Electron microscopic and biochemical studies of the effect of Gossypol on Ehrlich ascites tumor cells, *Caryologia, International Journal of Cytology, Cytosystematics and Cytogenetics* 35:114-115 (1982)
- de Peyster *et al.*, Genetic toxicity studies of gossypol, *Mutation Research* 197:293-312 (1993)
- De-yu *et al.*, Mutagenicity of gossypol analyzed by inductio of meiotic micronuclei in vitro, *Mutation Research* 208:69-72 (1988)
- Dhaliwal *et al.*, Cytogenetic Analysis of a Gossypol-Induced Murine Myxosarcoma, *Journal of the National Cancer Institute*, 78:1203-1209 (1987)
- A. Degterev *et al.*, *Nat. Cell Biolog.*, 3:173-182 (2001)
- Dogliotti *et al.*, Cytotoxic chemotherapy for adrenocortical carcinoma, *Minerva Endocrinologica*, 20:105-109 91995)
- Edwards *et al.*, Sysnthesis of Gossypol and Gossypol Derivatives, *Journal of the American Oil Chemists' Society* 47:441-442 (1970)
- Finaly *et al.*, Mechanism of the Gossypol Inactivation of Pepsinogen, *Journal of Biological Chemistry* 248:4827-4833 (1973)
- Fish *et al.*, The Photo-epimerisation of Gossypol Schiff's Bases, *Tetrahedron: Asymmetry* 6:873-876 (1995)
- Flack *et al.*, Treatment of adrenocortical carcinoma with gossypol, *Proceedings of American Association for Cancer Research* 31:198 (1990)
- Flack *et al.*, Oral Gossypol in the Treatment of Metastatic Adrenal Cancer, *Journal of Clinical Endocrinology and Metabolism*, 76:1019-1024 (1993)
- Floridi *et al.*, The Effect of the Association of Gossypol and Lonidamine on the Energy Metabolism of Ehrlich Ascites Tumor Cells, *Experimental and Molecular Pathology* 38:322-335 (1983)
- Floridi *et al.*, The Effect of Gossypol and Lonidamine on Electron Transport in Ehrlich Ascites Tumor Mitochondria, *Experimental and Molecular Pathology* 40:246-261 (1984)

- Ford *et al.*, Modulatio nof resistance of alkylating agents in cancer cell by gossypol enantiomers, *Cancer Letters* 56:85-94 91991)
- Gilbert *et al.*, Antiproliferative Activity of Gossypol and Gossypolone on Human Breast Cancer Cells, *Life Sciences* 57:61-67 (1995)
- Gonzalez-Garza *et al.*, Cytotoxic Effects of Gossypol and Vitamin E on Human and Rat Lymphocytes and Spermatozoa, *Nutrition Reports International* (1995)
- Gorczyca *et al.*, The Cell Cycle Related Differences in Susceptibility of HL-60 Cells to Apoptosis Induced by Various Antitumor Agents, *Cancer Research* 53:3186-3192 (1993)
- Grankvist, Gossypol-Induced Free Radical Toxicity to Isolated Islet Cells, *Int. J. Biochem.* 21:853-856 (1989)
- Hamasaki *et al.*, Gossypol, a potent inhibitor of arachidonate 5- and 12-lipoxygenases, *Biochimica et Biophysica Acta* 834:37-41 (1985)
- Han *et al.*, Gossypol in the Treatment of Endometriosis and Uterine Myoma, *Chontr. Gynec. Obstet.* 16:268-270 (1987)
- Haroz *et al.*, Tumor Initiating And Promoting Activity of Gossypol, *Toxicology letters*, 72 (1980)
- Haspel *et al.*, Cytocidal Effect of Gossypol on Cultured Murine Erythroleukemia Cells is Prevented by Serum Protein, *Journal of Pharmacology and Experimental Therapeutics* 229:218-225 (1984)
- J. Hirth *et al.*, *Clin. Cancer Res.*, 6:1255-1258 (2000)
- Heinstein *et al.*, The Biosynthesis of Gossypol, *Biochemistry* 28:1342-B (1967)
- Hendricks *et al.*, Hepatocarcinogenicity of Glandless Cottonseeds and Cottonseed Oil to Rainbow Trout (*Salmo gairdnerii*), *Science* 208:309-311 (1980)
- Herve *et al.*, Contraceptive gossypol blocks cell-to-cell communication in human and rat cells, *European Journal of Pharmacology* 313:243-255 (1966)
- Hong *et al.*, Study of the Effects of Acetate Gossypol, High Energy Shock Waves (HESW) and Their Combination on the Human Bladder Cancer Cell Line BT<sub>5637</sub>, *ACTA Anatomica Sinica* 25:291-296- (1994)

- Hu *et al.*, Gossypol Effects on Cultured Normal and Malignant Melanocytes, *In Vitro Cellular & Development Biology* 22:583-588 (1986)
- Hu *et al.*, Gossypol Inhibits Basal And Estrogen (E<sub>2</sub>)-Stimulated DNA Synthesis in Human Breast Carcinoma (HBC) Cells, *FASEB Journal*, 7:3982 (1993)
- Hu *et al.*, Gossypol Inhibits Basal And Estrogen-Stimulated DNA Synthesis in Human Breast Carcinoma Cells, *Life Sciences* 53:433-439 (1993)
- Hu *et al.*, Presence of antitumor activities in the milk collected from gossypol-treated dairy cows, *Cancer Letters* 87:17-23 (1994)
- Huang *et al.*, Resolution of Racemic Gossypol, *Journal of Ethnopharmacology* 20:13-20 (1987)
- Hutchinson *et al.*, The mechanism of gossypol acetic acid cytotoxicity, *Dissertation Abstracts International*, 59:1612-B (1998)
- Hutchinson *et al.*, Attenuation of Gossypol Cytotoxicity by Cyclic AMP in a Rat Liver Cell Line, *Toxicology and Applied Pharmacology* 151:311-318 (1998)
- Jaroszewski *et al.*, Action of Gossypol and Rhodamine 123 on Wild type and Multidrug-resistant MCF-7 Human Breast Cancer Cells: <sup>31</sup>P Nuclear Magnetic Resonance and Toxicity Studies, *Cancer Research* 50:6936-6943 (1990)
- Jarvis *et al.*, INduction of Apoptotic DNA Fragmentation and Cell Death in HL-60 Human Promyelocytic Leukemia Cells by Pharmacological Inhibitors of Protein Kinase C<sup>1</sup>, *Cancer Research* 54:1707-1714 (1994)
- Jiang *et al.*, Inhibitory Action of Gossypol on the Growth of MAT-LyLu Prostate Cancer Cells is Associated with Stimulation of Transforming Growth Factor-β<sub>1</sub> (TGF-β<sub>1</sub>), *Biology of Reproduction* 60:252
- Jiang *et al.*, Differing Effects of Gossypol on MAT-LYLU Cells and MAT-LYLU Cells Isolated From Metastasized Lung of MAT-LYLU Cell-Bearing Copenhagen Rats, *Society for the Study of Reproduction* 58:89
- Jiang *et al.*, The Efffects of Gossypol on the Invasiveness of MAT-LyLu Cells and MAT-LyLu Cells from the Metastasized Lungs of MAT-LyLu-Bearing Copenhagen Rats, *Anticancer Research* 20:4591-4598 (2000)

- Jia-xin *et al.*, Studies on the Synthesis of Gossypol Derivatives and Their Antifertility Action, Reproduction and Contraception 6:48:51 (1986)
- Joingfang *et al.*, Of Gossypol in Mice, Rats and Human Tumor Cell Lines and Its Possible Mechanism, ACTA Academiae Medicinae Sinicase 8:486-488 (1986)
- Jolad *et al.*, Tumor-Inhibitory Agent from *Montezuma speciosissima* (Malvaceae), Journal of Pharmaceutical Scicnes 64:1889-1890 (1975)
- Joseph *et al.*, Cytotoxicity of enantiomers of gossypol, Br. J. Cancer 54:511-513 (1986)
- Jung *et al.*, Recent Studies on Natural Products as Anti-HIV Agents, Current Medicinal Chemistry 7:649-651 (2000)
- Kai *et al.*, Resolution of Racemic Gossypol, J. Chem. Soc., Chem. Commun. 3:168:169 (1985)
- Kaplan *et al.*, Metabolism of breast cancer cells as revealed by non-invasive magnetic resonance spectroscopy studies, Breast Cancer Research and Treatment 31:285-299 (1994)
- Keller *et al.*, Novel pharmacophore-based methods reveal gossypol as a reverse transcriptase Inhibitor, Journal of Molecular Graphics and Modelling 5346:1-9 92002)
- Keniry *et al.*, Magnetic Resonance Spectroscopy (MRS) and Imaging (MRI) in the Evaluation of Tumor Growth and Chemotherapy Response, Proceedings of AACR 27:384 (1986)
- Keniry *et al.*, The Effect of Gossypol and 6-Aminonicotinamide on Tumor Cell Metabolism: A <sup>31</sup>P-Magnetic Resonance Spectroscopic Study, Biochemical and Biophysical Research Communications 164:947-953 (1989)
- Kim *et al.*, Comparative In Vitro Spermicidal Effects of (±)-Gossypol, (+)-Gossypol, (-)-Gossypol and Gossypolone, Contraception 30:253-259 (1984)
- Koll *et al.*, A Phase I Study of Gossypol (GP) in HIV-Infected Patients (pts) in Mexico, Abstracts of the 33rd ICAC 245-687
- Koryakin *et al.*, Ultrasound investigation of blood supply in scrotal organs, 10th World Congress on Human Reproduction 307 (1999)

- Latronico *et al.*, Extensive Personal Experience Adrenocortical Tumors, *Journal of Clinical Endocrinology and Metabolism* 82:1317-1324 (1997)
- LaVoie *et al.*, Investigation of Intracellular Signals Mediating the Anti-Apoptotic Action of Prolactin in Nb2 Lymphoma Cells, *Society for Experimental Biology and Medicine* 257:269 (1995)
- Lee, Novel Antitumor Agents from Higher Plants, *Medical Research Reviews*, 19:569-596 (1999)
- Lee *et al.*, Plant PHenolic Compounds as Cytotoxic Antitumor Agents, *American Chemical Society* 29:367-379 (1992)
- Lefeng *et al.*, Clincl Effects and Experimental Study on Gossypol in Endometriosis, *Chin. J. Integr Med.* 9(8):451-464 (1989)
- Levine, Inhibition of the A-23187-Stimulated Leukotriene And Prostaglandin Biosynthesis of Rat Basophil Leukemia (RBL-1) Cells By Non-Steroidal Anti-Inflammatory Drugs, Anti-Oxidants, and Calcium Channel Blockers, *Biochemical Pharmacology* 32:3023-3025 (1983)
- Li *et al.*, DNA-Breaking Versus DNA-Protecting Activity of Four Phenolic Compounds *in vitro*, *Free Rad. Res.* 33:551-566 (2000)
- Llian *et al.*, Hepatoma Initiating and Promoting Effects of Gossypol, *ACTA Academiae Medicinae Sinicase* (1985)
- Liang *et al.*, Developing gossypol derivatives with enhanced antitumor activity, *Investigational New Drugs* 13:181-186 (1995)
- Liqueros *et al.*, The antiproliferative Effects of Gossypol and the Retinoblastoma Gene Protein, *Clinical Pharmacology & therapeutics* 57:206 (1995)
- Liqueros *et al.*, Gossypol inhibition of mitosis, cyclin D1 and Rb protein in human mammary cancer cells and cyclin-D1 transfected human fibrosarcoma cells, *British Journal of Cancer* 76:(1):21-28 (1997)
- Lin *et al.*, Selective Inhibition of Human Immunodeficiency Virus Type 1 Replication by the (-) but Not the (+) Enantiomer of Gossypol, *Antimicrobial Agents and Chemotherapy*, 2149-2151 (1989)

- Lin *et al.*, Anti-HIV-1 Activity and Cellular Pharmacology of Various Analogs of Gossypol, *Biochemical Pharmacology* 46:251-255 (1993)
- Lin *et al.*, Gossypol and tamoxifen prevent estrogen-induced renal carcinogenesis in hamsters, *Proceedings of the American Association for Cancer Research* 36:391-2329 (1995)
- Majumdar *et al.*, Genotoxic Effects of Gossypol Acetic Acid on Cultured Murine Erythroleukemia Cells, *Environmental and Molecular Mutagenesis* 18:212-219 (1991)
- Matlin *et al.*, Large-Scale Resolution of Gossypol Enantiomers for Biological Evaluation, *Contraception* 37:229-237 (1988)
- McSheehy *et al.*, Gossypol, a cytotoxic agent, may uncouple respiration of Ehrlich ascites tumour cells, *Biochemical Society Transactions* 16:616-617 (1988)
- Meiling, Gossypol Treatment for Menopausal Functional Bleeding, Myoma of Uterus and Endometriosis - Preliminary Report, *ACTA Academiae Medicinae Sinicae* 2:167-169 (1980)
- Meltzer *et al.*, A Regioselective Route to Gossypol Analogues: The Synthesis of Gossypol and 5,5'-Didesisopropyl-5,5'-diethylgossypol, *J. Org. Chem.* 50:3121-3124 (1985)
- Fujii *et al.*, "Effect of cerulenin, an inhibitor of fatty acid synthesis, on the immune cytolysis of tumor cells" *Jpn. J. Exp. Med* 1986 Jun;56(3):99-106 (Abstract only)
- Gossypol, Xian Oil 7 Fat Works, *Drugs of the Future*, vol. 21, no. 5, 1996
- Meyers *et al.*, The synthesis of (S)-(+)-gossypol *via* an asymmetric Ullmann coupling, *Chem. Commun.*, 1573-1584 (1997)
- Moh *et al.*, Effect of Gossypol (GP) on a 5 $\alpha$ -Reductase and a 3 $\alpha$ -Hydroxysteroid Dehydrogenase (3 $\alpha$ -HSD) in Adult Rat Testes, *FASEB Journal* 6342 (1992)
- Mohan, Problems and Perspectives in the Design of Anti-HIV-1 Agents, *Drug Development Research* 29:1-17 (1993)
- S.W. Muchmore *et al.*, *Nature*, 381:335-341 (1996)). , and .

- Mushtaq *et al.*, Gossypol (GP) Inhibits in Vitro Porcine Oocyte Maturation and Early Embryonic Development in Modified Simple Media, Society for the Study of Reproduction, 52:172 (1998)
- Naik *et al.*, Preclinical studies of gossypol in prostate carcinoma, International Journal of Oncology 6:209-213 (1995)
- Nayak *et al.*, Induction of Sister Chromatid Exchanges and Chromosome Damage by Gossypol in Bone Marrow Cells of Mice, Teratogenesis, Carcinogenesis, and Mutagenesis 6:83-91 (1986)
- Newman *et al.*, Pharmacokinetics and toxicity of 120-hour continuous-infusion hydroxyurea in patients with advanced solid tumors, Cancer Chemotherapy Pharmacol 39:254-258 (1997)
- Ng *et al.*, Anti-Human Immunodeficiency virus (ANTI-HIV) Natural Products with Special Emphasis on HIV Reverse Transcriptase Inhibitors, Life Sciences 61:933-949 (1997)
- Ognyanov *et al.*, Synthesis of Gossypol Analogues, Helvetica Chimica ACTA 72:353-360 (1989)
- Ohuchi *et al.*, Inhibition of gossypol of tumor promoter-induced arachidonic acid metabolism in rat peritoneal macrophages, Biochimica et Biophysica Acta, 971:85-91 (1988)
- Olgiati *et al.*, Gossypol Inhibition of Adenylate Cyclase, Archives of Biochemistry and Biophysics 231:411-415 (1984)
- Papageorgiou *et al.*, A New Method for the Isolation of Gossypol From Cottonseed-Oil Fatty Acids, Chimika Chronika 7:101-109 (1978)
- Perez *et al.*, Studies on spermatogenesis and apoptosis in the bovine, Dissertation Abstracts International 50:526-B (1999)
- Phung *et al.*, Isolation and Purification of Gossypol in Cotton Seeds of Vietnam, Tap chi Hoa hov, 35:91-93 (1997)
- Pirogov *et al.*, Postoperative Bronchopleural Complications in Combined Treatment of Pulmonary Cancer, Issues of Oncology, 20:24-28 (1974)
- Polsky *et al.*, Inactivation of Human Immunodeficiency Virus (RIV) By Gossypol (GP), Clinical Research 35(3)487A (1987)

- Polsky *et al.*, Inactivation of Human Immunodeficiency Virus in Vitro by Gossypol, Contraception, 39:579-587 (1989)
- Rosenberg *et al.*, Biochemical Basis for the Gossypol-induced Inhibition of DNA Replication in Mammalian Cells, American Association for Cancer Research, 29:1291 (1988)
- Royer *et al.*, Inhibition of Human Immunodeficiency Virus Type I Replication by Derivatives of Gossypol, Pharmacological Research, 24:407-412 (1991)
- G. Rassidakis *et al.*, Amer. J. Path., 159:527-535 (2001)
- J.C. Reed *et al.*, Ann. Oncol., 5:61-65 (1994)
- Sampath *et al.*, A Rapid Procedure for the Resolution of Racemic Gossypol, J. Chem. Soc., Chem. Commun., 649-650 (1986)
- Schinazi *et al.*, Insights Into HIV Chemotherapy, Aids Research and Human Retroviruses, 8:963-990 (1992)
- A.F. Schott *et al.*, Oncogene, 11:1389-1394 (1995)
- Seidman *et al.*, Gossypol in Advanced Breast Cancer, Journal of Investigative Medicine 46:213A (1998)
- Seidman, Chemotherapy for Advanced Breast Cancer: A Current Perspective, Seminars in Oncology, 23:55-59 (1996)
- Shelly *et al.*, Stereo-specific cytotoxic effects of gossypol enantiomers and gossypolone in tumour cells lines, Cancer Letters, 135:171-180 (1999)
- Shelly *et al.*, Structure-activity studies on gossypol in tumor cell lines, Anti-Cancer Drugs, 11:209-216 (2000)
- S. Shi *et al.*, J. Histochem. Cytochem., 39:741-748 (1991)
- Shidaifat *et al.*, Differential regulation of gene expression by gossypol: A potential inhibitor of prostate cell growth, Dissertation Abstracts International, 57:6097-B (1997)
- Shidaifat *et al.*, Inhibition of human prostate cancer cells growth by gossypol is associated with stimulation of transforming growth factor- $\beta$ , Cancer Letters 107:37-44 (1996)
- Shidaifat *et al.*, Gossypol Arrests Human Benign Prostatic Hyperplastic Cell Growth at G0/G1 Phase of the Cell Cycle, Anticancer Research 17:1003-1010 (1997)

- Sinnhuber *et al.*, Dietary Factors and Hepatoma in Rainbow Trout (*Salmo gairdneri*). II. Cocarcinogenesis by Cyclopropenoid Fatty Acids and the Effect of Gossypol and Altered Lipids on Aflatoxin-Induced Liver Cancer, *Journal of the National Cancer Institute*, 41:1293-1299 (1968)
- Stein *et al.*, A preliminary clinical study of gossypol in advanced human cancer, *Cancer Chemother Pharmacol* 30:480-481 (1992)
- Sugimoto *et al.*, Differential proliferative responses to the (-)-enantiomer of gossypol in cultured human breast epithelial and stromal cells, *American Association for Cancer Research* 40:4 (1999)
- Tai, Rat Basophilic Leukemia-1 Cell Possesses 12-Lipoxygenase and 5-Lipoxygenase activities which are specifically inhibited by gossypol acetic acid, *Japanese Journal of Allergology* 33:1040-1046 (1984)
- Tan *et al.*, Evaluation of Natural Products As Inhibitors of Human Immunodeficiency Virus Type 1 (HIV-1) Reverse Transcriptase<sup>1</sup>, *Journal of Natural Products*, 54:143-154 (1991)
- Tanphaichitr *et al.*, Direct Effect of Gossypol on TR-ST Cells: Perturbation of Rhodamine 123 Accumulation in Mitochondria, *Biology of Reproduction*, 31:1049-1060 (1984)
- Tao *et al.*, The Effects of Gossypol on Human BPH Cells *In Vitro*, 21:31 (1994)
- Teng *et al.*, c-MYC Protein Expression in Spermatocytes During Gossypol-Induced Apoptosis, *Molecular Biology of the Cell*, 364a:2116 (1997)
- Teng *et al.*, Biphasic c-Myc Protein Expression During Gossypol-Induced Apoptosis in Rat Spermatocytes, *Contraception* 57:117-123 (1998)
- Teng, C-Fos Protein Expression in Apoptotic Rat Spermatocytes Induced by Gossypol, *Contraception* 57:281-286 (1998)
- Thoenes *et al.*, Cytotoxic Effects of Adriamycin, Bleomycin, Gossypol and Hydroxyanisole to Cultured Human Malignant Melanoma Cells, *Journal of Cancer Research and Clinical Oncology*, 113:D-THER:12, S46 (1987)
- Thomas *et al.*, Effects of Gossypol on the Cell Cycle Phases in T-47D Human Breast Cancer Cells, *Anticancer Research* 11:1469-1476 (1991)

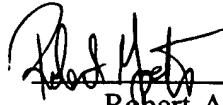
- Przybylski *et al.*, Spectroscopic studies and PM5 semiempirical calculations of new Schiff bases of gossypol with amino derivatives of crown ethers, *Journal of Molecular Structure*, 16:04-1-9 (2002)
- Qian, Gossypol: A Potential Antifertility Agent for Males, *Ann. Rev. Pharmacol. Toxicol.* 24:329-60 (1984)
- Qui *et al.*, The Search for Gene(s) Conferring Sensitivity to Cell Killing by Gossypol, *The FASEB Journal* 13:A151A (1999)
- J. O'Quigley *et al.*, *Biometrics* 46:33-48 (1990)
- Quintana *et al.*, Gossypol-induced DNA breaks in rat lymphocytes are secondary to cytotoxicity, *Toxicology Letters* 117:85-94 (2000)
- Rao *et al.*, Antitumor effects of gossypol on murine tumors, *Cancer Chemother Pharmacol.* 15:20-25 (1985)
- Razakantoanina *et al.*, Antimalarial activity of new gossypol derivatives, *Parasitol Res.* 86:665-668 (2000)
- Reidenberg, Studies of gossypol in the treatment of cancer, *Reproductive Medicine*, 305-308
- Reidenberg *et al.*, Gossypol Treatment of Metastatic Adrenal Cancer, *Clinical Pharmacology and Therapeutics*, 51:PI-96 (1992)
- Rekha *et al.*, Inhibition of Human Class 3 Aldehyde Dehydrogenase, and Sensitization of Tumor Cells that Express Significant Amounts of this Enzyme to Oxazaphosphorines, by the Naturally Occurring Compounds Gossypol, *Enzymology and Molecular Biology of Carbonyl Metabolism* 6, 133-146 (1996)
- Resnick *et al.*, Comparative Evaluation of Sperimicidal Agents with Virucidal Activity Against HIV, *IX<sup>th</sup> International Conference on AIDS*, 11:PO-C22-3154 (1993)
- D.K. Trask *et al.*, *Laryngoscope*, 112:638-644 (2002)
- Troll *et al.*, Free Oxygen Radicals: Necessary Contributors to Tumor Promotion and Cocarcinogenesis, *Proceedings of the 14th International Symposium of The Princess Takamatsu Cancer Research Fund*, 207-218 (1984)
- Tso, Gossypol Inhibits Ehrlich Ascites Tumor Cell Proliferation, *Cancer Letters* 24:257-261 (1984)

- Tuszynski *et al.*, Differential Cytotoxic Effect of Gossypol on Human Melanoma, Colon Carcinoma, and Other Tissue Culture Cell Lines, *Cancer Research* 44:768-771 (1984)
- Vander Jagt *et al.*, Gossypol: Prototype of Inhibitors Targeted to Dinucleotide Folds, *Current Medicinal Chemistry* 7:479-498 (2000)
- Van Poznak *et al.*, Oral Gossypol in the treatment of patients with refractory metastatic breast cancer: A phase I/II clinical trial, *Breast Cancer Research and Treatment* 66:239-248 (2001)
- Vlietinck *et al.*, Plant-Derived Leading Compounds for Chemotherapy of Human Immunodeficiency Virus (HIV) Injection, *PlantaMedica* 64:97-109 (1998)
- Wang *et al.*, Effect of Gossypol on DNA Synthesis and Cell Cycle Progression of Mammalian Cells *in Vitro*, *Cancer Research* 44:35-38 (1984)
- Wang *et al.*, Cytotoxic effect of gossypol on olonn carcinoma cells, *Life Sciences* 67:2663-2671 (2000)
- P. Watkins, *Pharmacogenetics*, 4:171-184 (1994)
- Wichmann *et al.*, Inhibiting herpes simplex virus tyupe 2 infection in human epithelial cells by gossypol, a potent spermicidal and contraceptive agent, *Am. J. Obstet. Gynecol.* 142:593-594 (1982)
- Wu *et al.*, Pharmacokinetics of (+)-, and (-)-, and (-)-gossypol in humans and dogs, *Clinical Pharmacology & Therapeutics* 39:613-618 (1996)
- Wu *et al.*, An *in Vitro* and *in Vivo* Study of Antitumor Effects of Gossypol on Human SW-13 Andrenocortical Carcinoma, *Cancer Research* 49:3743-3758 (1989)
- Wu *et al.*, In vitro antitumor activity of gossypol alone or in combination with amsacrine, *European Journal of Pharmacology* 183:230 (1990)
- Xueqing *et al.*, Clinical Observation and Experimental Study of Gossypol in Treatment of Dysfunctional Menorrhagia, Endometriosis and Fibromyoma of Uterus, *Chinese Journal of Integrated Traditional and Western Medicine* 8:197 (1988)

- Ye *et al.*, The Modulation of Gap Junctional Communication by Gossypol in Various Mammalian Cell Lines *in Vitro*, Fundamental And Applied Toxicology 14:817-832 (1990)
- Ye *et al.*, Toxicity of a Male Contraceptive, Gossypol, in Mammalian Cell Cultures, *In Vitro* 19:53-57 (1983)
- Yikang *et al.*, Studies on Resolution of Racemic Gossypol, Scientia Sinica 30:297-303 (1987)
- Ying *et al.*, Studies on Frequencies of Sister Chromatid Exchange in Peripheral Blood Lymphocytes Before and After Gossypol Treatment, Proc. DAMS and PUMC 1:34-36 (1986)
- Youfang *et al.*, Ultrastructural Changes of Smooth Muscle Cells in Leiomyoma and Myometrium of Human Uterus after Gossypol Treatment, ACTA Academiae Medicinae Sinicae, 9:299-301 (1987)
- Yu, Probing Into the Mechanism of Action, Metabolism and Toxicity of Gossypol by Studying its (+)- And (-)- Stereoisomers, Journal of Ethnopharmacology 20:65-78 (1987)
- Zhang *et al.*, The (-)-enantiomer of gossypol inhibits proliferation of stromal cells derived from human breast adipose tissues by enhancing transforming growth factor  $\beta_1$  production, International Journal of Oncology 13:1291-1297 (1998)

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: August 10, 2004



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FORM PTO-1449 (Modified)				U.S. Department of Commerce Patent and Trademark Office	Attorney Docket No.: UM-08477	Serial No.: 10/729,156	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (Use Several Sheets If Necessary) (37 CFR § 1.98(b))				Applicant: Shaomeng Wang <i>et al.</i>			
				Filing Date: 12/5/03		Group Art Unit:	

**U.S. PATENT DOCUMENTS**

Examiner Initials	Cite No.	Serial / Patent Number	Issue Date	Applicant / Patentee	Class	Subclass	Filing Date
	1	3,364,242	1/16/68	Johnson et al.	260	420	7/5/63
	2	3,347,885	10/17/67	Jones et al.	260	412.4	1/3/66
	3	4,297,341	10/27/81	Waller et al.	424	80	5/9/80
	4	4,747,979	5/31/88	Gimber et al.	260	412.4	2/14/85
	5	4,806,568	2/21/89	Vander Jagt et al.	514	522	9/12/95
	6	5,026,726	6/25/91	Jagt et al.	514	468	12/11/89
	7	5,059,717	10/22/91	Ibragimov et al.	568	438	7/16/90
	8	5,077,441	12/31/91	Kuk et al.	568	761	10/5/90
	9	5,112,637	5/12/92	Hron, Sr. et al.	426	629	11/5/90
	10	5,260,327	11/9/93	Kim et al.	514	405	8/4/92
	11	5,277,909	1/11/94	Schmidt et al.	424	195.1	8/24/90
	12	5,385,936	1/31/95	Flack et al.	514	548	7/12/90
	13	5,759,837	6/2/98	Kahajda et al.	435	193	1/24/94
	14	5,780,675	7/14/98	Royer et al.	562	467	4/28/95
	15	6,113,397	9/5/2000	Flack et al.	514	682	1/27/95
	16	6,576,660	6/10/03	Liao et al.	514	456	4/28/2000
	17	6,608,107	8/19/03	Wong et al.	514	548	12/14/01
	18	2002/0137801A1	9/26/02				
	19	2003/0082101A1	5/1/03				
	20	2003/0119894A1	6/26/03				

**FOREIGN PATENTS OR PUBLISHED FOREIGN PATENT APPLICATIONS**

		Document Number	Publication Date	Country / Patent Office	Class	Subclass	Translation	
							Yes	No
	21	WO 02/41828 A2	30 May 2002	PCT				
	22	WO 02/47673 A2	20 June 2002	PCT				
	23	EP 0 651 636 B1	26 July 1993	EP				
	24	1 917 341	3 April 1969	Germany				X
	25	01132542 A	19 Nov. 1987	Japan				
	26	CH 676360 A5	28/12/88	Switzerland				X
	27	SU 1351915 A1	16/6/82					X

Examiner: \_\_\_\_\_ Date Considered: \_\_\_\_\_

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<b>OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>			
	28	V. Amberger, <i>et al.</i> , Cancer Res., 58:149-158 (1998)	
	29	Wick <i>et al.</i> (W. Wick, <i>et al.</i> , FEBS Lett., 440:419-424 (1998))	
	30	S. Mohanam, <i>et al.</i> , Cancer Res. 53:4143-4147 (1993)	
	31	P. Pedersen, <i>et al.</i> , Cancer Res., 53:5158-5165 (1993)	
	32	Nuria Rubio, Lab Invest, 81:725-734 (2001)	
	33	Fernández <i>et al.</i> , Cell Death Differ., 7:350-359 (2000)	
	34	J. Reed, Nature, 387:773-776 (1997)	
	35	S. Frisch and E. Ruoslahti, Curr. Opin. Cell Biol., 9:701-706 ((1997))	
	36	D. Del Bufalo, <i>et al.</i> , FASEB J., 11:947-953 (1997)	
	37	Razakantoanina <i>et al.</i> Parasitol. Res., 86:665-668 (2000)	
	38	Dao <i>et al.</i> Bioorg. Med. Chem., 11:2001-2006 (2003)	
	39	Deck <i>et al.</i> J. Med. Chem., 34:3301-3305 (1991)	
	40	Przybylski <i>et al.</i> J. Mol. Structure, 611(1-3):193-201 (2002)	
	41	R.E. Royer <i>et al.</i> , J. Med. Chem., 38:2427-2432 (1995)	
	42	R.E. Royer <i>et al.</i> , "Biologically active derivatives of gossypol: synthesis and antimalarial activities of peri-acylated gossylic nitriles", J. Med. Chem., 29:1799-1801 (1986)	
	43	C.M. Venuti, J. Org. Chem., 46(15):3124-3127 (1981)	
	44	P.C. Meltzer <i>et al.</i> , J. Org. Chem., 50(17):3121-3124 (1985)	
	45	R. Adams <i>et al.</i> , J. Am. Chem. Soc., 60:2193-2204 (1938)	
	46	Le Blanc <i>et al.</i> "An in vitro study of inhibitory activity of gossypol, a cottonseed extract, in human carcinoma cell lines", Pharmacol. Res., 46:551-555 (2002)	
	47	Baumgrass <i>et al.</i> , "Reversible inhibition of calcineurin by the polyphenolic aldehyde gossypol", J. Biol. Chem., 276:47914-47921 (2001)	
	48	Shelley <i>et al.</i> , "Structure-activity studies on gossypol in tumor cell lines," Anticancer Drugs, 11:209-216 (2000)	
	49	Sonenberg <i>et al.</i> , "Anti-fertility and other reactions of gossypol analogues", Contraception, 37:247-255, (1988)	
	50	Whaley <i>et al.</i> "Monkey lactate dehydrogenase-C4 as a model for the interaction of enzymes with gossypol", Contraception, 33:605-616 (1986)	
	51	Dorsett <i>et al.</i> , "Letter: Antiviral activity of gossypol and apogossypol", J. Pharm. Sci., 64:1073-1075 (1975)	
	52	Wu <i>et al.</i> , "Synthesis and antifertility actions of gossypol derivatives and phenol aldehydes", Yao Xue Xue Bao, 24:502-511 (1989)	
	53	Hoffer <i>et al.</i> , "Antifertility, spermicidal and ultrastructural effects of gossypol and derivatives administered orally and by intratesticular injections", Contraception, 37:301-331 (1988)	
	54	Guo <i>et al.</i> , "Synthesis of mono-aldehyde gossypol and its analogues", Yao Xue Xue Bao, 22:597-602 (1987)	
	55	Manmade <i>et al.</i> , "Gossypol. Synthesis and in vitro spermicidal activity of isomeric hemigossypol derivatives", Experientia, 39:1276-1277 (1983)	
	56	Dowd, Chirality, 15:486 (2003)	
	57	Ciesielska <i>et al.</i> , Chem. Phys. Lett. 353:69 (2002)	
	58	Vermel <i>et al.</i> , Antitumour Activity of Gossypol in Experiments on Transplanted Tumours 39-43 (1963)	
	59	Freedman <i>et al.</i> , Chirality, 15:196 (2003)	
Examiner:		Date Considered:	
<b>EXAMINER:</b> Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

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<b>OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>			
	60	J.C. Reed, <i>Pharmacology</i> , 41:501-553 (1997)	
	61	J.C. Reed <i>et al.</i> , <i>J. Cell Biochem.</i> , 6:23-32 (1996)	
	62	Z. Han <i>et al.</i> , <i>Cancer Res.</i> , 56:621-628 (1996)	
	63	S.W. Muchmore <i>et al.</i> , <i>Nature</i> , 381:335-341 (1996)	
	64	A.M. Petros <i>et al.</i> , <i>Protein Sci.</i> , 9:2528-2534 (2000)	
	65	A.M. Petros <i>et al.</i> , <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 98:3012-3017 (2001)	
	66	X.M. Yin <i>et al.</i> , <i>Nature</i> , 369:321-323 (1994)	
	67	S.C. Cosulich <i>et al.</i> , <i>Curr. Biol.</i> , 7:913-920 (1997)	
	68	A. Sali <i>et al.</i> , <i>Structure, Function, and Genetics</i> , 23:318-326 (1995)	
	69	A. Sali, <i>Curr. Opin. Biotech.</i> , 6:437-451 (1995)	
	70	J.L. Wang <i>et al.</i> , <i>Cancer Res.</i> , 60:1498-1502 (2000)	
	71	J.L. Wang <i>et al.</i> , <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 97:7124-7129 (2000)	
	72	Sattler <i>et al.</i> , <i>Science</i> , 275:983-986 (1997)	
	73	B.R. Brooks <i>et al.</i> , <i>J. Comp. Chem.</i> , 4:187-217 (1983)	
	74	P.V.R. Schleyer <i>et al.</i> , CHARMM: The Energy Function and Its Parameterization with an Overview of the Program, in <i>The Encyclopedia of Computational Chemistry</i> , 1:271-277 eds., John Wiley & Sons, Chichester (1998)	
	75	S. Makino and I.D. Kuntz, <i>J. Comput. Chem.</i> 18:1812-1825 (1997)	
	76	I.J. Enyedy <i>et al.</i> , <i>J. Med. Chem.</i> , 44:313-4324 (2001)	
	77	Leschev, "Influence of the Extract of Eleutherococcus senticosus on development of experimental pituitary adenomas in rats", Institute of Oncology of the U.S.S.R. Academy of Medical Sciences, 60-67 (1966)	
	78	Willemse, An Oxazoline-Based Approach to the Total Asymmetric Synthesis of (S)-Gossypol, UMI PROQuest Digital Dissertations - Full Citation & Abstract	
	79	La Blanc <i>et al.</i> , An in vitro study of inhibitory activity of gossypol, a cottonseed extract, in human carcinoma cell lines, <i>Pharmacol. Res.</i> 46(6):551-5 (2002)	
	80	Griffith <i>et al.</i> , Bioenvision Successfully Completes Formulation Research to Develop Gossypol as a Novel Anti-Cancer Agent, <i>Bioenvision News</i> (2003)	
	81	Saydachmov <i>et al.</i> , Uebekskii Khimicheski Zhumal (1):11-13 (1994)	
	82	Zakhidov <i>et al.</i> , Modifying Cytogenetic Effects of Gossypol and Derivatives, Library National Institutes of Health (1994)	
	83	Yerukhimov, Treatment of Bladder Tumors With Gossypol And Ionol In Combination With Surgical Intervention, <i>Issues in Oncology</i> , XI (1966)	
	84	Kuznezova <i>et al.</i> , <i>Pharmacol. Toxicol.</i> , Boston Library Boston Spa (1979)	
	85	Zhong <i>et al.</i> , <i>National Library of Medicine</i> , 2:159-161 (1982)	
	86	Zhang <i>et al.</i> , Inhibitory effects (-)-gossypol on proliferation and keratinocyte growth factor expression in human breast epithelial cells, stromal cells, and adipocytes, <i>American Association for Cancer Research</i> 38:218 (1997)	
	87	Zheng <i>et al.</i> , Gossypol (GP) Stimulates Transforming Growth Factor Beta (TGF- $\beta$ ) Gene Expression in Human Breast Cancer Cell Line, <i>The FASEB Journal</i> 10:A757 (1996)	
	88	Zheng <i>et al.</i> , Studies on the Resolution of Racemic Gossypol, <i>ACTA Pharmaceutica Sinica</i> 25(6):430-434 (1990)	
Examiner:		Date Considered:	
<b>EXAMINER:</b> Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

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		Applicant: Shaomeng Wang <i>et al.</i> Filing Date: Group Art Unit:	
<b>OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>			
90	Adlakha <i>et al.</i> , Inhibition of DNA Polymerase $\alpha$ And Ribonucleotide Reductase by By Gossypol, Proceedings of AACR 26:249:982 (1985)		
91	Akhila <i>et al.</i> , Biosynthesis of Gossypol in <i>Thespesia Populnea</i> , Phytochemistry 33:335-340 (1993)		
92	Badria <i>et al.</i> , Antimitotic Activity of Gossypol and Gossypolone, Pharmaceutical Biology, 39:120-126 (2001)		
93	P. Baille <i>et al.</i> , Clin. Cancer Res., 3:1535-1538 (1997)		
94	Balci <i>et al.</i> , Gossypol induced apoptosis in the human promyelocytic cell line HL60, Cytogenet Cell Genet 85:5-181 (1999)		
95	Balci <i>et al.</i> , Gossypol Induced Apoptosis in the Human Promyelocytic Leukemia Cell Line HL 60, Tohoku J. Exp. Med. 189:51-57 (1999)		
96	Band <i>et al.</i> , Antiproliferative Effect Of Gossypol and Its Optical Isomers on Human Reproductive Cancer Cell Lines, Gynecologic Oncology 32:273-277 (1989)		
97	Band <i>et al.</i> , Cytocidal Effects of Gossypol and Its Optical Isomers on Reproductive Cancer Cell Lines, Gynecologic Oncology 23:261 (1986)		
98	Benz <i>et al.</i> , Lactic Dehydrogenase Isozymes, $^{31}\text{P}$ Magnetic Resonance Spectroscopy, and In Vitro Antimitochondrial Tumor Toxicity with Gossypol and Rhodamine-123, J. Clin. Invest. 79:517-523 (1987)		
99	Benz <i>et al.</i> , Selective Toxicity of Gossypol Against Epithelial Tumors and its Detection by Magnetic Resonance Spectroscopy, Contraception 37:221-229 (1988)		
100	Benz <i>et al.</i> , Gossypol Enantiomers (+, -) Differentially Uncouple Tumor Mitochondria, Block Glutathione-S-Transferase Acitivity, and Inhibit Cellular Proliferation, Proceedings of AACR 29:322 (1988)		
101	Benz <i>et al.</i> , Biochemical Correlates of the Antitumor and Antimitochondrial Properties of Gossypol Enantiomers, Molecular Pharmacology 37:840-847 (1990)		
91102	Benz <i>et al.</i> , Gossypol Effects on Endothelial Cells and Tumor Flow, Life Sciences 49:67-72 (1991)		
103	Blackstaffe <i>et al.</i> , Cytotoxicity of gossypol enantiomers and its quinone metabolite gossypolone in melanoma cell lines, Melanoma Research 7:364-372 (1997)		
104	Bourinbaiar <i>et al.</i> , Comparative in vitro study of contraceptive agents with anti-HIV activity: <i>Gramicidin, nonoxynol-9, and gossypol</i> , Contraception 49:131-137 (1994)		
105	Brandes <i>et al.</i> , New Drugs in Recurrent High Grade Gliomas, Anticancer Research 20:1913-1920 (2000)		
106	Brandes <i>et al.</i> , New therapeutic agents in the treatment of recurrent high-grade gliomas, FORUM Trends in Experimental and Clinical Medicine 10:121-131 (2000)		
107	R. Bruno <i>et al.</i> , J. Clin. Oncol., 16:187-196 (1998)		
108	Bushunow <i>et al.</i> , Gossypol Treatment of Recurrent Adult Malignant-Gliomas, Proceedings of ASCO, 14:282 (1995)		
109	Bushunow <i>et al.</i> , Gossypol Treatment of recurrent adult malignant gliomas, Journal of Neuro-Oncology 43:79-86 (1999)		
110	Chang <i>et al.</i> , Antiproliferative and Antimetastatic Effects of Gossypol (GP) on Mat-LyLu-Bearing Rats, FASEB Journal, 6:3794 (1992)		
111	Chang <i>et al.</i> , Prostate, begin hypertrophy and prostatic carcinoma: A study of cell biology of prostate and chemotherapy for prostatic hypertrophy and prostatic cancer, Dissertation Abstract International, 55:4330-B (1995)		
112	Chang <i>et al.</i> , Potential of Gossypol (GP) and Transforming Growth Factor- $\beta$ , (TGF- $\beta$ ) as Inhibitors of Canine Prostate Growth, FASEB Journal, 9:4813-4814 (1995)		
113	Chang <i>et al.</i> , Antiproliferative and Antimetastatic Effects of Gossypol on Dunning Prostate Cell-Bearing Copenhagen Rats, Research Communications in Chemical Pathology and Pharmacology 79:293-312 (1993)		
114	Chen <i>et al.</i> , Application of 2D NMR Techniques in the Structure Determination of Ganosporelactone A and B, ACTA Pharmaceutica Sinica 26:430-436 (1991)		
115	Coyle <i>et al.</i> , <i>In-Vitro</i> and <i>in vivo</i> cytotoxicity of gossypol against central nervous system tumor cell lines, Journal of Neur-Oncology 19:25-35 (1994)		
116	Dallacker <i>et al.</i> , Über Gossypol- und Hemigossypol-Derivate - Darstellung von Hydroxy-methyl-naphto[1,3]dioxolen, Chemiker-Zeitung 113:5-11 (1989)		
Examiner:		Date Considered:	
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		Applicant: Shaomeng Wang <i>et al.</i> Filing Date: Group Art Unit:	
<b>OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>			
	117	Dallacker <i>et al.</i> , Darstellung von Methyl-isopropyl-naphthol-derivaten durch Pd-katalysierte Cyclocarbonylierung, Chemiker-Zeitung 114:144-147 (1990)	
	118	Dao <i>et al.</i> , Synthesis and cytotoxicity of gossypol related compounds, Eur. J. Med. Chem. 35:805-813 (2000)	
	119	Darzynkiewicz <i>et al.</i> , Cytometry in Cell Necrobiology: Analysis of Apoptosis and Accidental Cell Death (Necrosis), Cytometry 27:1-20 (1997)	
	120	Data <i>et al.</i> , A Study of the Derivatives of (+)-Gossypol, Indian Journal of Chemistry 10:691-693 (1972)	
	121	Davila <i>et al.</i> , Toxicological Studies of Gossypol in Primary Culture of Postnatal Rat Hepatocytes, Journal of Molecular and Cellular Toxicology, 4:161-170 (1991)	
	123	Deck <i>et al.</i> , Gossypol and Derivatives: A New Class of Aldose Reductase Inhibitors, J. Med. Chem. 34:3301-3305 (1991)	
	124	DeMartino <i>et al.</i> , Electron microscopic and biochemical studies of the effect of Gossypol on Ehrlich ascites tumor cells, Caryologia, International Journal of Cytology, Cytosystematics and Cytogenetics 35:114-115 (1982)	
	125	de Peyster <i>et al.</i> , Genetic toxicity studies of gossypol, Mutation Research 197:293-312 (1993)	
	126	De-yu <i>et al.</i> , Mutagenicity of gossypol analyzed by inductio of meiotic micronuclei in vitro, Mutation Research 208:69-72 (1988)	
	127	Dhaliwal <i>et al.</i> , Cytogenetic Analysis of a Gossypol-Induced Murine Myxosarcoma, Journal of the National Cancer Institute, 78:1203-1209 (1987)	
	128	A. Degterev <i>et al.</i> , Nat. Cell Biolog., 3:173-182 (2001)	
	129	Dogliotti <i>et al.</i> , Cytotoxic chemotherapy for adrenocortical carcinoma, Minerva Endocrinologica, 20:105-109 91995)	
	130	Edwards <i>et al.</i> , Sysnthesis of Gossypol and Gossypol Derivatives, Journal of the American Oil Chemists' Society 47:441-442 (1970)	
	131	Finaly <i>et al.</i> , Mechanism of the Gossypol Inactivation of Pepsinogen, Journal of Biological Chemistry 248:4827-4833 (1973)	
	132	Fish <i>et al.</i> , The Photo-epimerisation of Gossypol Schiff's Bases, Tetrahedron: Asymmetry 6:873-876 (1995)	
	133	Flack <i>et al.</i> , Treatment of adrenocortical carcinoma with gossypol, Proceedings of American Association for Cancer Research 31:198 (1990)	
	134	Flack <i>et al.</i> , Oral Gossypol in the Treatment of Metastatic Adrenal Cancer, Journal of Clinical Endocrinology and Metabolism, 76:1019-1024 (1993)	
	135	Floridi <i>et al.</i> , The Effect of the Association of Gossypol and Lonidamine on the Energy Metabolism of Ehrlich Ascites Tumor Cells, Experimental and Molecular Pathology 38:322-335 (1983)	
	136	Floridi <i>et al.</i> , The Effect of Gossypol and Lonidamine on Electron Transport in Ehrlich Ascites Tumor Mitochondria, Experimental and Molecular Pathology 40:246-261 (1984)	
	137	Ford <i>et al.</i> , Modulatio nof resistance of alkylating agents in cancer cell by gossypol enantiomers, Cancer Letters 56:85-94 91991)	
	138	Gilbert <i>et al.</i> , Antiproliferative Activity of Gossypola nd Gossypolone on Human Breast Cancer Cells, Life Sciences 57:61-67 (1995)	
	139	Gonzalez-Garza <i>et al.</i> , Cytotoxic Effects of Gossypol and Vitamin E on Human and Rat Lymphocytes and Spermatozoa, Nutrition Reports International (1995)	
	140	Gorczyca <i>et al.</i> , The Cell Cycle Related Differences in Susceptibility of HL-60 Cells to Apoptosis Induced by Various Antitumor Agents, Cancer Research 53:3186-3192 (1993)	
	141	Grankvist, Gossypol-Induced Free Radical Toxicity to Isolated Islet Cells, Int. J. Biochem. 21:853-856 (1989)	
	142	Hamasaki <i>et al.</i> , Gossypol, a potent inhibitor of arachidonate 5- and 12-lipoxygenases, Biochimica et Biophysica Acta 834:37-41 (1985)	
	143	Han <i>et al.</i> , Gossypol in the Treatment of Endometriosis and Uterine Myoma, Chontr. Gynec. Obstet. 16:268-270 (1987)	
	144	Haroz <i>et al.</i> , Tumor Initiating And Promoting Activity of Gossypol, Toxicology letters, 72 (1980)	
	145	Haspel <i>et al.</i> , Cytocidal Effect of Gossypol on Cultured Murine Erythroleukemia Cells is Prevented by Serum Protein, Journal of Pharmacology and Experimental Therapeutics 229:218-225 (1984)	
Examiner:		Date Considered:	
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		Applicant: Shaomeng Wang <i>et al.</i> Filing Date: Group Art Unit:	
<b>OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>			
	146	J. Hirth <i>et al.</i> , Clin. Cancer Res., 6:1255-1258 (2000)	
	147	Heinstein <i>et al.</i> , The Biosynthesis of Gossypol, Biochemistry 28:1342-B (1967)	
	148	Hendricks <i>et al.</i> , Hepatocarcinogenicity of Glandless Cottonseeds and Cottonseed Oil to Rainbow Trout ( <i>Salmo gairdneri</i> ), Science 208:309-311 (1980)	
	149	Herve <i>et al.</i> , Contraceptive gossypol blocks cell-to-cell communication in human and rat cells, European Journal of Pharmacology 313:243-255 (1966)	
	150	Hong <i>et al.</i> , Study of the Effects of Acetate Gossypol, High Energy Shock Waves (HESW) and Their Combination on the Human Bladder Cancer Cell Line BT <sub>5637</sub> , ACTA Anatomica Sinica 25:291-296- (1994)	
	151	Hu <i>et al.</i> , Gossypol Effects on Cultured Normal and Malignant Melanocytes, In Vitro Cellular & Development Biology 22:583-588 (1986)	
	152	Hu <i>et al.</i> , Gossypol Inhibits Basal And Estrogen (E <sub>2</sub> )-Stimulated DNA Synthesis in Human Breast Carcinoma (HBC) Cells, FASEB Journal, 7:3982 (1993)	
	153	Hu <i>et al.</i> , Gossypol Inhibits Basal And Estrogen-Stimulated DNA Synthesis in Human Breast Carcinoma Cells, Life Sciences 53:433-439 (1993)	
	154	Hu <i>et al.</i> , Presence of antitumor activities in the milk collected from gossypol-treated dairy cows, Cancer Letters 87:17-23 (1994)	
	155	Huang <i>et al.</i> , Resolution of Racemic Gossypol, Journal of Ethnopharmacology 20:13-20 (1987)	
	156	Huchinson <i>et al.</i> , The mechanism of gossypol acetic acid cytotoxicity, Dissertation Abstracts International, 59:1612-B (1998)	
	157	Hutchinson <i>et al.</i> , Attenuation of Gossypol Cytotoxicity by Cyclic AMP in a Rat Liver Cell Line, Toxicology and Applied Pharmacology 151:311-318 (1998)	
	158	Jaroszewski <i>et al.</i> , Action of Gossypol and Rhodamine 123 on Wild type and Multidrug-resistant MCF-7 Human Breast Cancer Cells: <sup>31</sup> P Nuclear Magnetic Resonance and Toxicity Studies, Cancer Research 50:6936-6943 (1990)	
	159	Jarvis <i>et al.</i> , INDuction of Apoptotic DNA Fragmentation and Cell Death in HL-60 Human Promyelocytic Leukemia Cells by Pharmacological Inhibitors of Protein Kinase C', Cancer Research 54:1707-1714 (1994)	
	160	Jiang <i>et al.</i> , Inhibitory Action of Gossypol on the Growth of MAT-LyLu Prostate Cancer Cells is Associated with Stimulation of Transforming Growth Factor- $\beta_1$ (TGF- $\beta_1$ ), Biology of Reproduction 60:252	
	161	Jiang <i>et al.</i> , Differing Effects of Gossypol on MAT-LYLU Cells and MAT-LYLU Cells Isolated From Metastasized Lung of MAT-LYLU Cell-Bearing Copenhagen Rats, Society for the Study of Reproduction 58:89	
	162	Jiang <i>et al.</i> , The Effects of Gossypol on the Invasiveness of MAT-LyLu Cells and MAT-LyLu Cells from the Metastasized Lungs of MAT-LyLu-Bearing Copenhagen Rats, Anticancer Research 20:4591-4598 (2000)	
	163	Jia-xin <i>et al.</i> , Studies on the Synthesis of Gossypol Derivatives and Their Antifertility Action, Reproduction and Contraception 6:48:51 (1986)	
	164	Joingsfang <i>et al.</i> , Of Gossypol in Mice, Rats and Human Tumor Cell Lines and Its Possible Mechanism, ACTA Academiae Medicinae Sinicase 8:486-488 (1986)	
	165	Jolad <i>et al.</i> , Tumor-Inhibitory Agent from <i>Montezuma speciosissima</i> (Malvaceae), Journal of Pharmaceutical Sciences 64:1889-1890 (1975)	
	166	Joseph <i>et al.</i> , Cytotoxicity of enantiomers of gossypol, Br. J. Cancer 54:511-513 (1986)	
	167	Jung <i>et al.</i> , Recent Studies on Natural Products as Anti-HIV Agents, Current Medicinal Chemistry 7:649-651 (2000)	
	168	Kai <i>et al.</i> , Resolution of Racemic Gossypol, J. Chem. Soc., Chem. Commun. 3:168:169 (1985)	
	168	Kaplan <i>et al.</i> , Metabolism of breast cancer cells as revealed by non-invasive magnetic resonance spectroscopy studies, Breast Cancer Research and Treatment 31:285-299 (1994)	
	170	Keller <i>et al.</i> , Novel pharmacophore-based methods reveal gossypol as a reverse transcriptase inhibitor, Journal of Molecular Graphics and Modelling 5346:1-9 92002)	
Examiner:		Date Considered:	
<b>EXAMINER:</b> Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

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<b>OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>			
171	Keniry <i>et al.</i> , Magnetic Resonance Spectroscopy (MRS) and Imaging (MRI) in the Evaluation of Tumor Growth and Chemotherapy Response, <i>Proceedings of AACR</i> 27:384 (1986)		
172	Keniry <i>et al.</i> , The Effect of Gossypol and 6-Aminonicotinamide on Tumor Cell Metabolism: A <sup>31</sup> P-Magnetic Resonance Spectroscopic Study, <i>Biochemical and Biophysical Research Communications</i> 164:947-953 (1989)		
173	Kim <i>et al.</i> , Comparative <u>In Vitro</u> Spermicidal Effects of (+)-Gossypol, (+)-Gossypol, (-)-Gossypol and Gossypolone, <i>Contraception</i> 30:253-259 (1984)		
174	Koll <i>et al.</i> , A Phase I Study of Gossypol (GP) in HIV-Infected Patients (pts) in Mexico, <i>Abstracts of the 33rd ICAC</i> 245-687		
175	Koryakin <i>et al.</i> , Ultrasound investigation of blood supply in scrotal organs, <i>10th World Congress on Human Reproduction</i> 307 (1999)		
176	Latronico <i>et al.</i> , Extensive Personal Experience Adrenocortical Tumors, <i>Journal of Clinical Endocrinology and Metabolism</i> 82:1317-1324 (1997)		
177	LaVoie <i>et al.</i> , Investigation of Intracellular Signals Mediating the Anti-Apoptotic Action of Prolactin in Nb2 Lymphoma Cells, <i>Society for Experimental Biology and Medicine</i> 257:269 (1995)		
178	Lee, Novel Antitumor Agents from Higher Plants, <i>Medical Research Reviews</i> , 19:569-596 (1999)		
179	Lee <i>et al.</i> , Plant Phenolic Compounds as Cytotoxic Antitumor Agents, <i>American Chemical Society</i> 29:367-379 (1992)		
180	Lefeng <i>et al.</i> , Clinical Effects and Experimental Study on Gossypol in Endometriosis, <i>Chin. J. Integr Med.</i> 9(8):451-464 (1989)		
181	Levine, Inhibition of the A-23187-Stimulated Leukotriene And Prostaglandin Biosynthesis of Rat Basophil Leukemia (RBL-1) Cells By Non-Steroidal Anti-Inflammatory Drugs, Anti-Oxidants, and Calcium Channel Blockers, <i>Biochemical Pharmacology</i> 32:3023-3025 (1983)		
182	Li <i>et al.</i> , DNA-Breaking Versus DNA-Protecting Activity of Four Phenolic Compounds <i>in vitro</i> , <i>Free Rad. Res.</i> 33:551-566 (2000)		
183	Llian <i>et al.</i> , Hepatoma Initiating and Promoting Effects of Gossypol, <i>ACTA Academiae Medicinae Sinicae</i> (1985)		
184	Liang <i>et al.</i> , Developing gossypol derivatives with enhanced antitumor activity, <i>Investigational New Drugs</i> 13:181-186 (1995)		
185	Liquerous <i>et al.</i> , The antiproliferative Effects of Gossypol and the Retinoblastoma Gene Protein, <i>Clinical Pharmacology &amp; therapeutics</i> 57:206 (1995)		
186	Liquerous <i>et al.</i> , Gossypol inhibition of mitosis, cyclin D1 and Rb protein in human mammary cancer cells and cyclin-D1 transfected human fibrosarcoma cells, <i>British Journal of Cancer</i> 76:(1):21-28 (1997)		
187	Lin <i>et al.</i> , Selective Inhibition of Human Immunodeficiency Virus Type 1 Replication by the (-) but Not the (+) Enantiomer of Gossypol, <i>Antimicrobial Agents and Chemotherapy</i> , 2149-2151 (1989)		
188	Lin <i>et al.</i> , Anti-HIV-1 Activity and Cellular Pharmacology of Various Analogs of Gossypol, <i>Biochemical Pharmacology</i> 46:251-255 (1993)		
189	Lin <i>et al.</i> , Gossypol and tamoxifen prevent estrogen-induced renal carcinogenesis in hamsters, <i>Proceedings of the American Association for Cancer Research</i> 36:391-2329 (1995)		
190	Majumdar <i>et al.</i> , Genotoxic Effects of Gossypol Acetic Acid on Cultured Murine Erythroleukemia Cells, <i>Environmental and Molecular Mutagenesis</i> 18:212-219 (1991)		
191	Matlin <i>et al.</i> , Large-Scale Resolution of Gossypol Enantiomers for Biological Evaluation, <i>Contraception</i> 37:229-237 (1988)		
192	McSheehy <i>et al.</i> , Gossypol, a cytotoxic agent, may uncouple respiration of Ehrlich ascites tumour cells, <i>Biochemical Society Transactions</i> 16:616-617 (1988)		
193	Meiling, Gossypol Treatment for Menopausal Functional Bleeding, Myoma of Uterus and Endometriosis - Preliminary Report, <i>ACTA Academiae Medicinae Sinicae</i> 2:167-169 (1980)		
194	Meltzer <i>et al.</i> , A Regioselective Route to Gossypol Analogues: The Synthesis of Gossypol and 5,5'-Didesisopropyl-5,5'-diethylgossypol, <i>J. Org. Chem.</i> 50:3121-3124 (1985)		
195	Fujii <i>et al.</i> , "Effect of cerulenin, an inhibitor of fatty acid synthesis, on the immune cytotoxicity of tumor cells" <i>Jpn. J. Exp. Med</i> 1986 Jun;56(3):99-106 (Abstract only)		
196	Gossypol, Xian Oil 7 Fat Works, <i>Drugs of the Future</i> , vol. 21, no. 5, 1996		
197	Meyers <i>et al.</i> , The synthesis of (S)-(+)gossypol via an asymmetric Ullmann coupling, <i>Chem. Commun.</i> , 1573-1584 (1997)		
Examiner:		Date Considered:	
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		Serial No.: Applicant: Shaomeng Wang <i>et al.</i>	
		Filing Date: _____	
<b>OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>			
198	Moh <i>et al.</i> ... Effect of Gossypol (GP) on a 5 $\alpha$ -Reductase and a 3 $\alpha$ -Hydroxysteroid Dehydrogenase (3 $\alpha$ -HSD) in Adult Rat Testes, FASEB Journal 6:342 (1992)		
199	Mohan, Problems and Perspectives in the Design of Anti-HIV-1 Agents, Drug Development Research 29:1-17 (1993)		
200	S.W. Muchmore <i>et al.</i> , Nature, 381:335-341 (1996). , and .		
201	Mushtaq <i>et al.</i> , Gossypol (GP) Inhibits in Vitro Porcine Oocyte Maturation and Early Embryonic Development in Modified Simple Media, Society for the Study of Reproduction, 52:172 (1998)		
202	Naik <i>et al.</i> , Preclinical studies of gossypol in prostate carcinoma, International Journal of Oncology 6:209-213 (1995)		
203	Nayak <i>et al.</i> , Induction of Sister Chromatid Exchanges and Chromosome Damage by Gossypol in Bone Marrow Cells of Mice, Teratogenesis, Carcinogenesis, and Mutagenesis 6:83-91 (1986)		
204	Newman <i>et al.</i> , Pharmacokinetics and toxicity of 120-hour continuous-infusion hydroxyurea in patients with advanced solid tumors, Cancer Chemother Pharmacol 39:254-258 (1997)		
205	Ng <i>et al.</i> , Anti-Human Immunodeficiency virus (ANTI-HIV) Natural Products with Special Emphasis on HIV Reverse Transcriptase Inhibitors, Life Sciences 61:933-949 (1997)		
206	Ognyanov <i>et al.</i> , Synthesis of Gossypol Analogues, Helvetica Chimica ACTA 72:353-360 (1989)		
207	Ohuchi <i>et al.</i> , Inhibition of gossypol of tumor promoter-induced arachidonic acid metabolism in rat peritoneal macrophages, Biochimica et Biophysica Acta, 971:85-91 (1988)		
208	Olgiati <i>et al.</i> , Gossypol Inhibition of Adenylate Cyclase, Archives of Biochemistry and Biophysics 231:411-415 (1984)		
209	Papageorgiou <i>et al.</i> , A New Method for the Isolation of Gossypol From Cottonseed-Oil Fatty Acids, Chimika Chronika 7:101-109 (1978)		
210	Perez <i>et al.</i> , Studies on spermatogenesis and apoptosis in the bovine, Dissertation Abstracts International 50:526-B (1999)		
211	Phung <i>et al.</i> , Isolation and Purification of Gossypol in Cotton Seeds of Vietnam, Tap chi Hoa hov, 35:91-93 (1997)		
212	Pirogov <i>et al.</i> , Postoperative Bronchopleural Complications in Combined Treatment of Pulmonary Cancer, Issues of Oncology, 20:24-28 (1974)		
213	Polsky <i>et al.</i> , Inactivation of Human Immunodeficiency Virus (RIV) By Gossypol (GP), Clinical Research 35(3):487A (1987)		
214	Polsky <i>et al.</i> , Inactivation of Human Immunodeficiency Virus in Vitro by Gossypol, Contraception, 39:579-587 (1989)		
215	Przybylski <i>et al.</i> , Spectroscopic studies and PM5 semiempirical calculations of new Schiff bases of gossypol with amino derivatives of crown ethers, Journal of Molecular Structure, 16:04-1-9 (2002)		
216	Qian, Gossypol: A Potential Antifertility Agent for Males, Ann. Rev. Pharmacol. Toxicol. 24:329-60 (1984)		
217	Qui <i>et al.</i> , The Search for Gene(s) Conferring Sensitivity to Cell Killing by Gossypol, The FASEB Journal 13:A151A (1999)		
218	J. O'Quigley <i>et al.</i> , Biometrics 46:33-48 (1990)		
219	Quintana <i>et al.</i> , Gossypol-induced DNA breaks in rat lymphocytes are secondary to cytotoxicity, Toxicology Letters 117:85-94 (2000)		
220	Rao <i>et al.</i> , Antitumor effects of gossypol on murine tumors, Cancer Chemother Pharmacol. 15:20-25 (1985)		
221	Razakantoanina <i>et al.</i> , Antimalarial activity of new gossypol derivatives, Parasitol Res. 86:665-668 (2000)		
222	Reidenberg, Studies of gossypol in the treatment of cancer, Reproductive Medicine, 305-308		
223	Reidenberg <i>et al.</i> , Gossypol Treatment of Metastatic Adrenal Cancer, Clinical Pharmacology and Therapeutics, 51:PI-96 (1992)		
224	Rekha <i>et al.</i> , Inhibition of Human Class 3 Aldehyde Dehydrogenase, and Sensitization of Tumor Cells that Express Significant Amounts of this Enzyme to Oxazaphosphorines, by the Naturally Occurring Compounds Gossypol, Enzymology and Molecular Biology of Carbonyl Metabolism 6, 133-146 (1996)		
225	Resnick <i>et al.</i> , Comparative Evaluation of Spermidical Agents with Virucidal Activity Against HIV, IX <sup>th</sup> International Conference on AIDS, 11:PO-C22-3154 (1993)		
Examiner:		Date Considered:	
<b>EXAMINER:</b> Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

FORM PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office	Attorney Docket No.: UM-08477	Serial No.:
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## OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

226	Rosenberg <i>et al.</i> , Biochemical Basis for the Gossypol-induced Inhibition of DNA Replication in Mammalian Cells, American Association for Cancer Research, 29:1291 (1988)
227	Royer <i>et al.</i> , Inhibition of Human Immunodeficiency Virus Type I Replication by Derivatives of Gossypol, Pharmacological Research, 24:407-412 (1991)
228	G. Rassidakis <i>et al.</i> , Amer. J. Path., 159:527-535 (2001)
229	J.C. Reed <i>et al.</i> , Ann. Oncol., 5:61-65 (1994)
230	Sampath <i>et al.</i> , A Rapid Procedure for the Resolution of Racemic Gossypol, J. Chem. Soc., Chem. Commun., 649-650 (1986)
231	Schinazi <i>et al.</i> , Insights Into HIV Chemotherapy, Aids Research and Human Retroviruses, 8:963-990 (1992)
232	A.F. Schott <i>et al.</i> , Oncogene, 11:1389-1394 (1995)
234	Seidman <i>et al.</i> , Gossypol in Advanced Breast Cancer, Journal of Investigative Medicine 46:213A (1998)
235	Seidman, Chemotherapy for Advanced Breast Cancer: A Current Perspective, Seminars in Oncology, 23:55-59 (1996)
236	Shelly <i>et al.</i> , Stereo-specific cytotoxic effects of gossypol enantiomers and gossypolone in tumour cells lines, Cancer Letters, 135:171-180 (1999)
237	Shelly <i>et al.</i> , Structure-activity studies on gossypol in tumor cell lines, Anti-Cancer Drugs, 11:209-216 (2000)
238	S. Shi <i>et al.</i> , J. Histochem. Cytochem., 39:741-748 (1991)
239	Shidaifat <i>et al.</i> , Differential regulation of gene expression by gossypol: A potential inhibitor of prostate cell growth, Dissertation Abstracts International, 57:6097-B (1997)
240	Shidaifat <i>et al.</i> , Inhibition of human prostate cancer cells growth by gossypol is associated with stimulation of transforming growth factor- $\beta$ , Cancer Letters 107:37-44 (1996)
241	Shidaifat <i>et al.</i> , Gossypol Arrests Human Benign Prostatic Hyperplastic Cell Growth at G0/G1 Phase of the Cell Cycle, Anticancer Research 17:1003-1010 (1997)
242	Sinnhuber <i>et al.</i> , Dietary Factors and Hepatoma in Rainbow Trout ( <i>Salmo gairdneri</i> ). II. Cocarcinogenesis by Cyclopropenoid Fatty Acids and the Effect of Gossypol and Altered Lipids on Aflatoxin-Induced Liver Cancer, Journal of the National Cancer Institute, 41:1293-1299 (1968)
243	Stein <i>et al.</i> , A preliminary clinical study of gossypol in advanced human cancer, Cancer Chemother Pharmacol 30:480-481 (1992)
244	Sugimoto <i>et al.</i> , Differential proliferative responses to the (-)-enantiomer of gossypol in cultured human breast epithelial and stromal cells, American Association for Cancer Research 40:4 (1999)
245	Tai, Rat Basophilic Leukemia-1 Cell Possesses 12-Lipoxygenase and 5-Lipoxygenase activities which are specifically inhibited by gossypol acetic acid, Japanese Journal of Allergology 33:1040-1046 (1984)
246	Tan <i>et al.</i> , Evaluation of Natural Products As Inhibitors of Human Immunodeficiency Virus Type I (HIV-1) Reverse Transcriptase <sup>1</sup> , Journal of Natural Products, 54:143-154 (1991)
247	Tanphaichitr <i>et al.</i> , Direct Effect of Gossypol on TR-ST Cells: Perturbation of Rhodamine 123 Accumulation in Mitochondria, Biology of Reproduction, 31:1049-1060 (1984)
248	Tao <i>et al.</i> , The Effects of Gossypol on Human BPH Cells <i>In Vitro</i> , 21:31 (1994)
249	Teng <i>et al.</i> , c-MYC Protein Expression in Spermatocytes During Gossypol-Induced Apoptosis, Molecular Biology of the Cell, 364a:2116 (1997)
250	Teng <i>et al.</i> , Biphasic c-Myc Protein Expression During Gossypol-Induced Apoptosis in Rat Spermatocytes, Contraception 57:117-123 (1998)
251	Teng, C-Fos Protein Expression in Apoptotic Rat Spermatocytes Induced by Gossypol, Contraception 57:281-286 (1998)
252	Thoenes <i>et al.</i> , Cytotoxic Effects of Adriamycin, Bleomycin, Gossypol and Hydroxyanisole to Cultured Human Malignant Melanoma Cells, Journal of Cancer Research and Clinical Oncology, 113:D-THER:12, S46 (1987)
253	Thomas <i>et al.</i> , Effects of Gossypol on the Cell Cycle Phases in T-47D Human Breast Cancer Cells, Anticancer Research 11:1469-1476 (1991)

Examiner:

Date Considered:

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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<b>OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>					
	254	D.K. Trask <i>et al.</i> , Laryngoscope, 112:638-644 (2002)			
	255	Troll <i>et al.</i> , Free Oxygen Radicals: Necessary Contributors to Tumor Promotion and Cocarcinogenesis, Proceedings of the 14th International Symposium of The Princess Takamatsu Cancer Research Fund, 207-218 (1984)			
	256	Tso, Gossypol Inhibits Ehrlich Ascites Tumor Cell Proliferation, Cancer Letters 24:257-261 (1984)			
	257	Tuszynski <i>et al.</i> , Differential Cytotoxic Effect of Gossypol on Human Melanoma, Colon Carcinoma, and Other Tissue Culture Cell Lines, Cancer Research 44:768-771 (1984)			
	258	Vander Jagt <i>et al.</i> , Gossypol: Prototype of Inhibitors Targeted to Dinucleotide Folds, Current Medicinal Chemistry 7:479-498 (2000)			
	259	Van Poznak <i>et al.</i> , Oral Gossypol in the treatment of patients with refractory metastatic breast cancer: A phase I/II clinical trial, Breast Cancer Research and Treatment 66:239-248 (2001)			
	260	Vlietinck <i>et al.</i> , Plant-Derived Leading Compounds for Chemotherapy of Human Immunodeficiency Virus (HIV) Injection, PlantaMedica 64:97-109 (1998)			
	261	Wang <i>et al.</i> , Effect of Gossypol on DNA Synthesis and Cell Cycle Progression of Mammalian Cells <i>in Vitro</i> , Cancer Research 44:35-38 (1984)			
	262	Wang <i>et al.</i> , Cytotoxic effect of gossypol on olonn carcinoma cells, Life Sciences 67:2663-2671 (2000)			
	263	P. Watkins, Pharmacogenetics, 4:171-184 (1994)			
	264	Wichmann <i>et al.</i> , Inhibiting herpes simplex virus type 2 infection in human epithelial cells by gossypol, a potent spermicidal and contraceptive agent, Am. J. Obstet. Gynecol. 142:593-594 (1982)			
	265	Wu <i>et al.</i> , Pharmacokinetics of (+)-, and (+)-, and (-)-gossypol in humans and dogs, Clinical Pharmacology & Therapeutics 39:613-618 (1996)			
	266	Wu <i>et al.</i> , An <i>in Vitro</i> and <i>in Vivo</i> Study of Antitumor Effects of Gossypol on Human SW-13 Andrenocortical Carcinoma, Cancer Research 49:3743-3758 (1989)			
	267	Wu <i>et al.</i> , In vitro antitumor activity of gossypol alone or in combination with amsacrine, European Journal of Pharmacology 183:230 (1990)			
	268	Xueqing <i>et al.</i> , Clinical Observation and Experimental Study of Gossypol in Treatment of Dysfunctional Menorrhagia, Endometriosis and Fibromyoma of Uterus, Chinese Journal of Integrated Traditional and Western Medicine8:197 (1988)			
	269	Ye <i>et al.</i> , The Modulation of Gap Junctional Communication by Gossypol in Various Mammalian Cell Lines <i>in Vitro</i> , Fundamental And Applied Toxicology 14:817-832 (1990)			
	270	Ye <i>et al.</i> , Toxicity of a Male Contraceptive, Gossypol, in Mammalian Cell Cultures, In Vitro 19:53-57 (1983)			
	271	Yikang <i>et al.</i> , Studies on Resolution of Racemic Gossypol, Scientia Sinica 30:297-303 (1987)			
	272	Ying <i>et al.</i> , Studies on Frequencies of Sister Chromatid Exchange in Peripheral Blood Lymphocytes Before and After Gossypol Treatment, Proc. DAMS and PUMC 1:34-36 (1986)			
	273	Youfang <i>et al.</i> , Ultrastructural Changes of Smooth Muscle Cells in Leiomyoma and Myometrium of Human Uterus after Gossypol Treatment, ACTA Academiae Medicinae Sinicae, 9:299-301 (1987)			
	274	Yu, Probing Into the Mechanism of Action, Metabolism and Toxicity of Gossypol by Studying its (+)- And (-)- Stereoisomers, Journal of Ethnopharmacology 20:65-78 (1987)			
	275	Zhang <i>et al.</i> , The (-)-enantiomer of gossypol inhibits proliferation of stromal cells derived from human breast adipose tissues by enhancing transforming growth factor $\beta_1$ production, International Journal of Oncology 13:1291-1297 (1998)			
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